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THE LACK OF CONSISTENT DIASPIRIN CROSS-LINKED HEMOGLOBIN INFUSION BLOOD PRESSURE EFFECTS IN THE US AND EU TRAUMATIC HEMORRHAGIC SHOCK CLINICAL TRIALS

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ABSTRACT—Hemoglobin solutions have demonstrated a pressor effect that could adversely affect hemorrhagic shock patient resuscitation through accelerated hemorrhage, diminished perfusion, or inadequate resuscitation. Data from two parallel, multicenter traumatic hemorrhagic shock clinical trials in 17 US emergency departments and in 27 EU prehospital systems using diaspirin cross-linked hemoglobin (DCLHb), a hemoglobin-based resuscitation fluid. In the 219 patients, patients were 37 years old, 64% sustained blunt injury, 48% received DCLHb, and 36% expired. Although mean systolic blood pressure (SBP) and diastolic blood pressure values differed at 2 of the 10 measured time points, blood pressure (BP) curve analysis showed no SBP, diastolic blood pressure, or MAP differences based on treatment. Although SBP values 160 and 120 mmHg or greater were 2.2× and 2.6× more frequently noted in survivors, they were not more common with DCLHb use or in DCLHb patients who expired in US study nonsurvivors or in any EU study patients. Systolic blood pressure values 160 and 120 mmHg or greater were 2.8× and 1.3× more frequently noted in DCLHb survivors as compared with normal saline survivors. Only 3% of the BP variation noted could be attributed to DCLHb use, and as expected, injury severity and baseline physiologic status were stronger predictors. In the United States alone, treatment group was not correlated by regression with BP at any time point. Neither mean BP readings nor elevated BP readings were correlated with DCLHb treatment of traumatic hemorrhagic shock patients. As such, no clinically demonstrable DCLHb pressor effect could be directly related to the adverse mortality outcome observed in the US study.

KEYWORDS—Diaspirin cross-linked hemoglobin, traumatic hemorrhagic shock, blood pressure, resuscitation, mortality, pressor effect

INTRODUCTION

Patients sustaining traumatic hemorrhagic shock have had an unacceptably high mortality rate despite optimal resuscitation efforts (1–4). For many years, there has been a search for hemoglobin-based oxygen carriers (HBOCs) that could be used as a resuscitation fluid both in the battlefield and in the civilian settings (5–7). Many of the solutions have demonstrated a pressor effect that is manifested by increased blood pressure (BP) both during and after the time of infusion (8–19). This pressor effect could have a deleterious effect on patient outcome if it adversely alters perfusion to vital organs, accelerates hemorrhage in the setting of vascular or solid organ injury, or causes patients to be inadequately resuscitated due to the normalization of BP.

The study of diaspirin cross-linked hemoglobin (DCLHb) in traumatic hemorrhagic shock patients included two parallel studies in the US emergency departments and in the EU prehospital setting (20, 21). Because DCLHb is a pure tetrameric hemoglobin solution, it is of particular interest when considering pressor effects (22, 23). In fact, it was tested in clinical studies not only as an oxygen carrier but also as a therapeutic agent that could enhance vital organ tissue perfusion (17, 24).

Recent interest in the pressor effects of DCLHb in these traumatic hemorrhagic clinical trials has arisen in part because of ongoing efforts to test HBOC-201 in a similar prehospital hemorrhagic shock clinical trial (25–29). The lack of a beneficial effect of DCLHb in these trials is highlighted due to the results of the PolyHeme prehospital traumatic hemorrhagic shock clinical trial, which also did not demonstrate a beneficial mortality effect (30–32).

This study determined if DCLHb use caused a pressor effect that was consistently correlated with elevated BPs over time and the occurrence of systolic BP values greater than 120 and 160 mmHg. This information will assist future traumatic hemorrhagic shock resuscitation study design efforts by maximizing safety related to infusion volumes, rates, and BP mortality. It will also support the use of the exception to informed consent, when indicated, in these important traumatic hemorrhagic shock clinical trials.

MATERIALS AND METHODS

The clinical trials of DCLHb in traumatic hemorrhagic shock occurred between February 1997 and January 1998 in the United States and from July

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14. ABSTRACT

Hemoglobin solutions have demonstrated a pressor effect that could adversely affect hemorrhagic shock patient resuscitation through accelerated hemorrhage, diminished perfusion, or inadequate resuscitation. Data from two parallel, multicenter traumatic hemorrhagic shock clinical trials in 17 US emergency departments and in 27 EU prehospital systems using diaspirin cross-linked hemoglobin (DCLHb), a hemoglobin-based resuscitation fluid. In the 219 patients patients were 37 years old, 64% sustained blunt injury, 48% received DCLHb, and 36% expired. Although mean systolic blood pressure (SBP) and diastolic blood pressure values differed at 2 of the 10 measured time points, blood pressure (BP) curve analysis showed no SBP, diastolic blood pressure, or MAP differences based on treatment. Although SBP values 160 and 120 mmHg or greater were 2.2x and 2.6x more frequently noted in survivors, they were not more common with DCLHb use or in DCLHb patients who expired in US study nonsurvivors or in any EU study patients. Systolic blood pressure values 160 and 120 mmHg or greater were 2.8x and 1.3x more frequently noted in DCLHb survivors as compared with normal saline survivors. Only 3% of the BP variation noted could be attributed to DCLHb use, and as expected, injury severity and baseline physiologic status were stronger predictors. In the United States alone, treatment group was not correlated by regression with BP at any time point. Neither mean BP readings nor elevated BP readings were correlated with DCLHb treatment of traumatic hemorrihagic shock patients. As such, no clinically demonstrable DCLHb pressor effect could be directly related to the adverse mortality outcome observed in the US study.

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1997 to May 1998 in the EU study (20, 21). Because of an observed increased mortality in the DCLHb-treated patients in the US study, this study was terminated by the Data Safety Monitoring Board after the enrollment of 98 patients, and the EU study was also halted after the enrollment of 121 patients.

The database for the current analysis of BP after DCLHb use in traumatic hemorrhagic shock came from the original data sets that were collected by Baxter Healthcare for the US and EU studies. Blood pressure data were obtained for each patient in the US trial at enrollment (Entry); at 30, 60, 90, and 120 min; and after 2, 3, and 4 U resuscitation fluid infusion, which correspond to mean times of 46, 62, 66 min, respectively. In the EU trial, BP values were obtained at Entry; at 15, 30, 45, 60, 90, and 120 min; and after 2-, 3-, and 4-U time points for those who received DCLHb. The combined data set contains data from 219 patients at these 10 collection time points.

The statistical analysis of the BP data included the calculation and the comparison of mean and SD data, comparing the BP curves for BP, and comparing the distribution of patients who had elevated systolic blood pressure (SBP) readings of 160 and 120 mmHg or greater in the different treatment and outcome groups. A random intercept mixed model was used to compare the BP curves over time. Regression analysis was used to determine whether the use of DCLHb influenced BP over time and to what extend that influence was noted as compared with baseline demographic, injury severity, and physiological variables. Final patient survival status (lived versus died) was based on the 28-day mortality. For the five patients whose final outcome was not determined, it was assumed that they survived to 28 days.

The protocols used in US and EU clinical trials were approved by the institutional review board of each participating institution before the enrollment of any subjects. Trials were conducted in compliance with all regulations for good clinical trials and practice. The US study was conducted under federal regulations governing emergency research with an exception to informed consent. The current analysis of the data was conducted with institutional review board approval from the University of Illinois at Chicago.

RESULTS

There were a total of 219 patients studied, with 55% coming from the EU study (Table 1). The mean age was 37.3 years, 64% of the patients sustained a blunt injury, 48% received DCLHb resuscitation, and the overall mortality rate was 36.5%.

Using a random intercept mixed model, data showed no significant difference in SBP, diastolic blood pressure (DBP), or MAP values over time based on treatment group in this combined data set. Systolic blood pressure differed at only two specific time points based on treatment group (Fig. 1A). At the 15-min time point, DCLHb-treated patients had a higher mean SBP (97 vs. 84 mmHg, $P < 0.03$), and at the after 2-U time point, normal saline (NS)–treated patients had a higher mean SBP (117 vs. 105 mmHg, $P < 0.04$). Diastolic blood pressure also differed at only two time points based on treatment group (Fig. 1B). At the after 4-U time point, NS-treated patients had a higher mean DBP (72 vs. 44 mmHg, $P < 0.05$), and at the 120-min time point, DCLHb-treated patients had a higher mean DBP (67 vs. 60 mmHg, $P < 0.03$). Mean MAP values did not differ at any time points based on treatment group (Fig. 1C).

Systolic blood pressure values 160 and 120 mmHg or greater did not differ by treatment group in either study or in the combined data set (Table 2). The only observed trend toward higher SBP values in DCLHb-treated patients was the observation of more SBP values 160 mmHg or greater (3.9% vs. 2.1%, $P < 0.06$). Higher SBP readings were consistently noted in patients who survived as compared with those who died. Systolic blood pressure values 160 mmHg or greater were 2.2× more often observed in patients who survived (3.8 vs. 1.7%, $P < 0.05$), and SBP values 120 mmHg or greater were 2.6× more likely in the survival group (37 vs. 14%, $P <$ 0.001). Similar differences were noted based on survival status in each study individually.

TABLE 1. **Patient demographics and clinical variables in the US and EU DCLHb clinical trials**

Age (years), mean ± SD	37.3 ± 17.2
Gender, n (%)	
Male	159 (72.6%)
Female	60 (27.4%)
Study setting, n (%)	
United States	98 (44.7%)
European Union	121 (55.3%)
Resuscitation fluid, n (%)	
DCLHb	106 (48.4%)
NS	113 (51.6%)
Injury mechanism, n (%)	
Blunt	139 (63.5%)
Penetrating	80 (36.5%)
Blunt injury type, n (%)	
Motor vehicle crash	94 (67.6%)
Fall	32 (23.0%)
Other	13 (9.4%)
Penetrating injury type, n (%)	
Gun shot wound	35 (43.8%)
Stab wound	27 (33.8%)
Other	11 (13.8%)
Motor vehicle crash	6 (7.5%)
Fall	1 (1.3%)
ISS, mean ± SD	30.4 ± 18.1
28-Day outcome, n (%)	
Survived	139 (63.5%)
Expired	80 (36.5%)

Although patients who expired did not sustain elevated SBPs more frequently, those who lived were observed to more frequently have elevated SBPs when treated with DCLHb (Table 3). Systolic blood pressure values 160 mmHg or greater were 2.8× more common (5.8 vs. 2.1%, $P < 0.008$), and SBP values 120 mmHg or greater were 1.3× more common (42 vs. 33%, $P < 0.007$) in DCLHb-treated patients who lived when compared with NS patients who lived. Regardless of treatment group, again it was observed that patients who survived as opposed to those who expired were more likely to have SBP readings 160 and 120 mmHg or greater. DCLHb survivors were 3.6× and 2.7× more likely to have SBPs 160 and 120 mmHg or greater, respectively. NS-treated patients who survived were 2.9× more likely to have elevated SBP readings at the 120-mmHg or greater cutoff.

When comparing BP values based on outcome, it was noted using a random intercept mixed model that SBP, DBP, and MAP values all were higher over time in survivors (Fig. 2, A–C). Mean SBP values were also higher for survivors at all 10 time points (Fig. 2A). Diastolic blood pressure and MAP values were both higher at 6 of the 10 recorded time points in

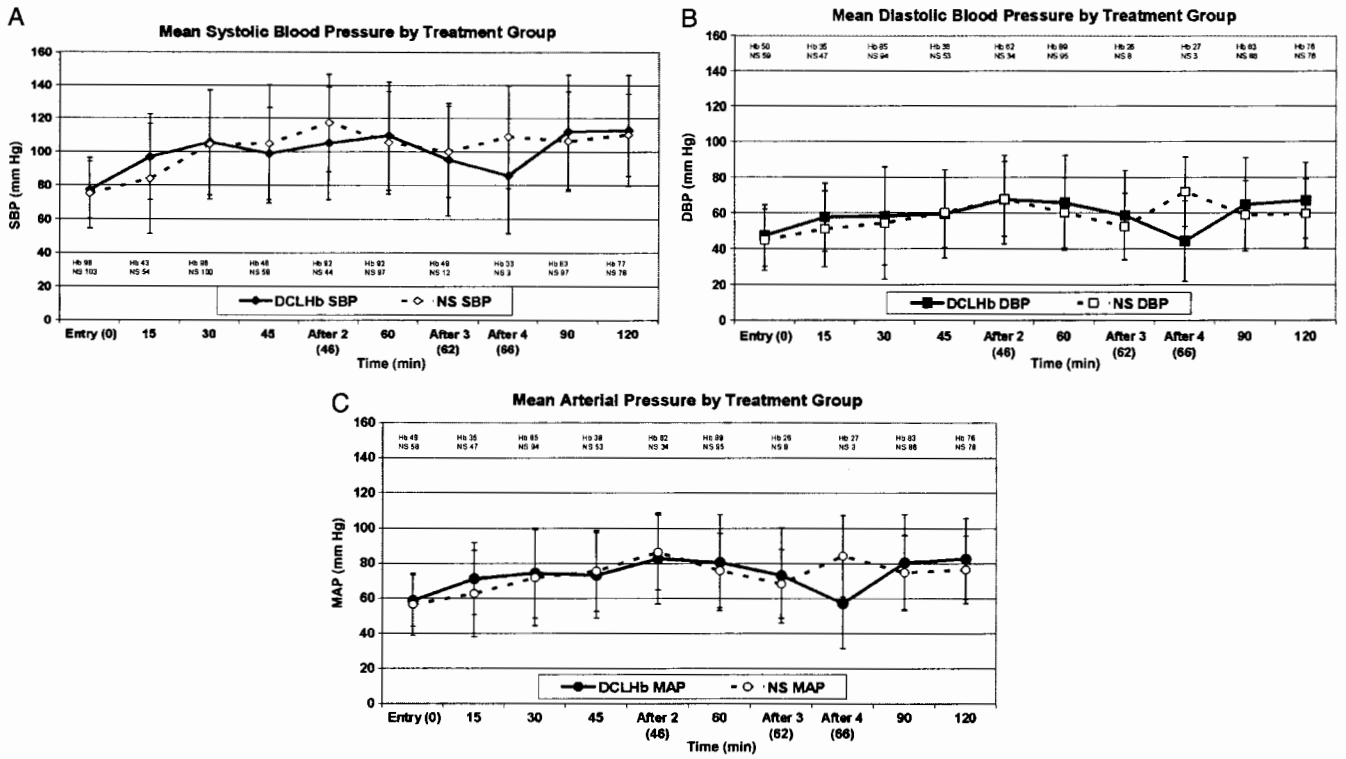

FIG. 1. **Blood pressure by treatment group in the US and EU DCLHb clinical trials.** A, Mean SBP by treatment group. B, Mean DBP by treatment group. C, MAP by treatment group.

survivors (Fig. 2, B and C). Given the observed BP differences based on outcome, a separate analysis examined mean BP values over time based on patient outcome and treatment group (Figs. 3, A–C and 4, A–C). In survivors, SBP was different at only one time point, with DCLHb survivors having a higher SBP at 90 min (125 vs. 113 mmHg, $P < 0.003$; Fig. 3A). Diastolic blood pressure and MAP values were higher in DCLHb-treated survivors only at the 60-, 90-, and 120-min time points, with all observed differences being 12 mmHg or less (Fig. 3, B and C).

In patients who expired because of their traumatic hemorrhagic shock, there were no significant SBP, DBP, or MAP differences at any time points based on treatment group (Fig. 4, A–C).

Given the higher observed mortality in DCLHb-treated patients only in the US study, this survivor/treatment group analysis was also performed for the US and EU studies individually. In the US study survivors, DCLHb-treated patients had higher mean SBP and MAP values at four time points, and DBP values were higher at three time points (Fig. 5, A–C). In US study patients who expired, no SBP, DBP, or MAP differences were observed (Fig. 6, A–C). In the EU study, there were no differences in the mean BP values in the DCLHb-treated patients as compared with the NS-treated patients at any time points when analyzed in aggregate or based on outcome. In the combined data set from both studies, regression analysis demonstrated that SBP at only the after 2-U infused (46 min) time point was significantly related to treatment group (coefficient = 12.17 ± 5.92, $P < 0.05$). Six other clinically relevant variables were found to be more strongly correlated with SBP at this time, including injury severity score (ISS), revised trauma score (RTS), emergency department (ED), Glasgow Coma scale (GCS) score, surgery requirement, and initial base deficit. As such, only 3.1% of the

TABLE 2. **Elevated SBP values in the US and EU DCLHb clinical trials**

Study	SBP ≥ 160 mmHg	*P*	SBP ≥ 120 mmHg	*P*
Combined				
DCLHb	28/711 (3.9%)	0.06	216/711 (30.4%)	ns
NS	13/634 (2.1%)		175/634 (27.6%)	
US trial				
DCLHb	15/320 (4.7%)	ns	127/320 (39.7%)	ns
NS	7/275 (2.6%)		99/275 (36.0%)	
EU trial				
DCLHb	13/391 (3.3%)	ns	89/391 (22.8%)	ns
NS	6/359 (1.7%)		76/359 (21.2%)	
Combined				
Survived	33/871 (3.8%)	0.05	324/871 (37.2%)	<0.001
Died	8/474 (1.7%)		67/474 (14.1%)	
US trial				
Survived	16/397 (4.0%)	ns	188/397 (47.4%)	<0.001
Died	6/198 (3.0%)		38/198 (19.2%)	
EU trial				
Survived	17/474 (3.6%)	0.03	136/474 (28.7%)	<0.001
Died	2/276 (0.72%)		29/276 (10.5%)	

TABLE 3. **Elevated SBP values based on treatment group and survival status**

Study	SBP ≥ 160 mmHg	*P*	SBP ≥ 120 mmHg	*P*
Combined				
DCLHb	28/711 (3.9%)	0.06	216/711 (30.4%)	ns
NS	13/634 (2.1%)		175/634 (27.6%)	
All patients who died				
DCLHb	5/312 (1.6%)	ns	48/312 (15.4%)	ns
NS	3/162 (1.9%)		19/162 (11.47)	
All patients who lived				
DCLHb	23/399 (5.8%)	0.008	168/399 (42.1%)	0.007
NS	10/472 (2.1%)		156/472 (33.1%)	
Combined				
Survived	33/871 (3.8%)	0.05	324/871 (37.2%)	<0.001
Died	8/474 (1.7%)		67/474 (14.1%)	
All DCLHb patients				
Survived	23/399 (5.8%)	0.008	168/399 (42.1%)	<0.001
Died	5/312 (1.6%)		48/312 (15.4%)	
All NS patients				
Survived	10/472 (2.1%)	ns	156/472 (33.1%)	<0.001
Died	3/162 (1.9%)		19/162 (11.4%)	

variation in the SBP at this time point could be attributed to treatment group. In the combined data set, DBP was correlated with treatment group at 120 min only (coefficient = -7.29 ± 3.28, $P < 0.05$). Again, only 3.2% of the variation was attributed to treatment group, with five other clinical variables being more strongly correlated to DBP at this time point: ISS, preinfusion Hb level, preinfusion heart rate, RTS, and ED GCS score. MAP at 120 min was also weakly correlated with treatment group (coefficient = -6.80 ± 3.29, $P < 0.05$). Variation due to treatment group was 2.8%, with seven clinical variables being more strongly correlated with MAP at this time point: preinfusion Hb level, ISS, entry heart rate,

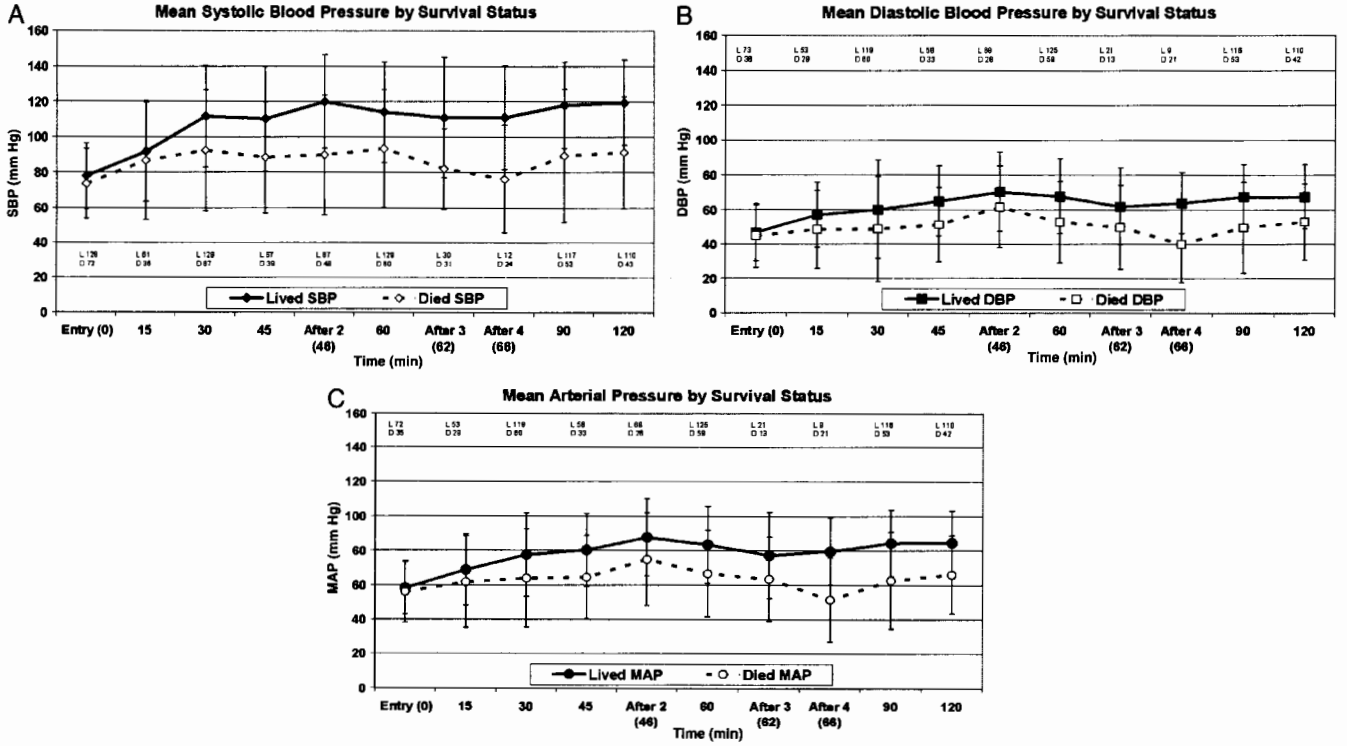

FIG. 2. **Blood pressure by survival status in the US and EU DCLHb clinical trials.** A, Mean SBP by survival status. B, Mean DBP by survival status. C, MAP by survival status.

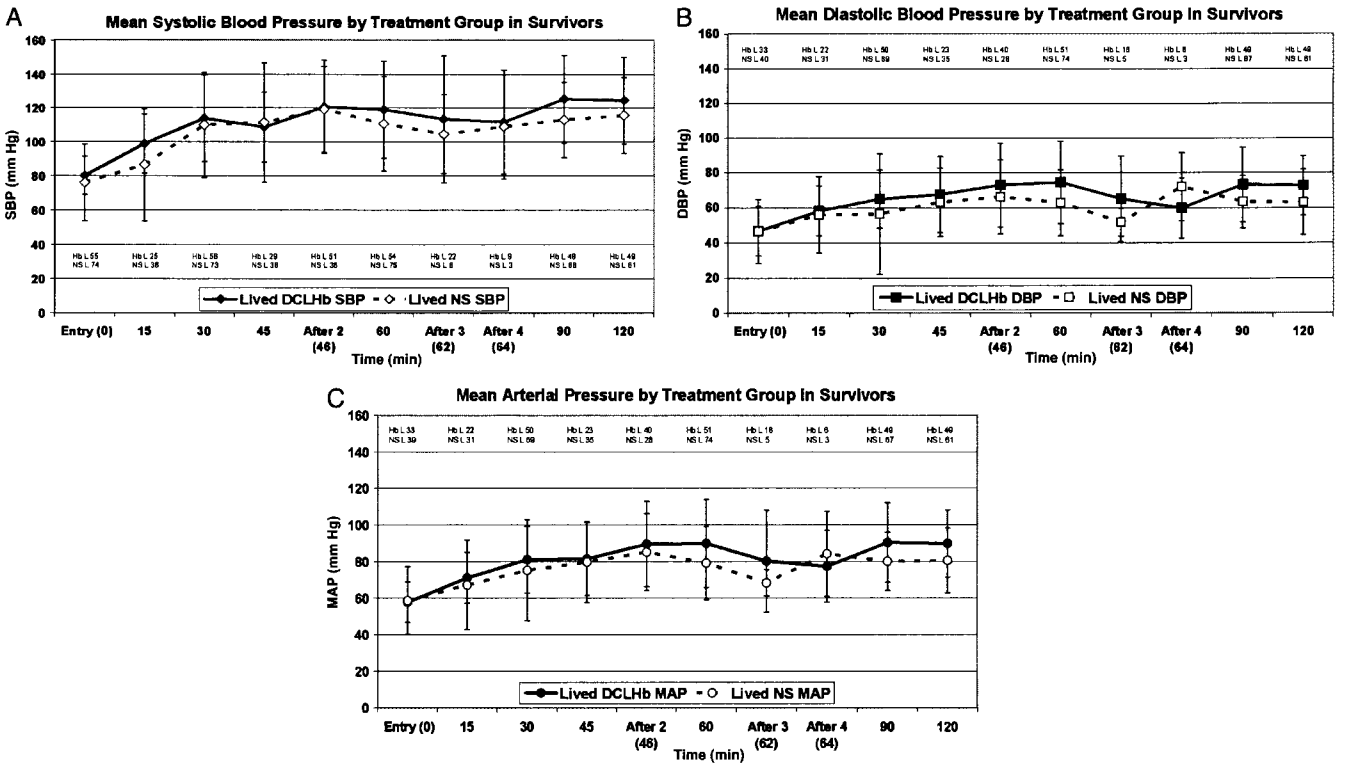

FIG. 3. **Blood pressure by treatment group in survivors in the US and EU DCLHb clinical trials.** A, Mean SBP by treatment group in survivors. B, Mean DBP by treatment group in survivors. C, MAP by treatment group in survivors.

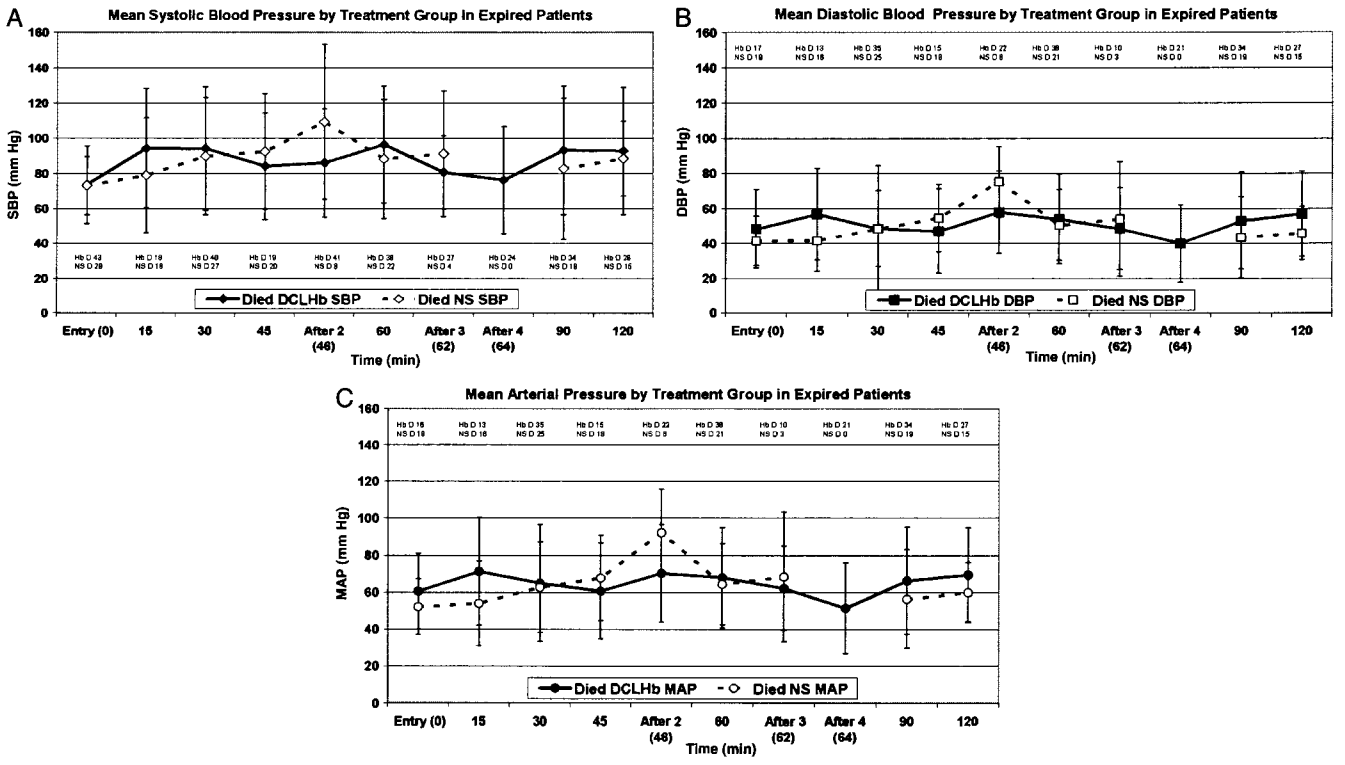

FIG. 4. **Blood pressure by treatment group in expired patients in the US and EU DCLHb clinical trials.** A, Mean SBP by treatment group in expired patients. B, Mean DBP by treatment group in expired patients. C, MAP by treatment group in expired patients.

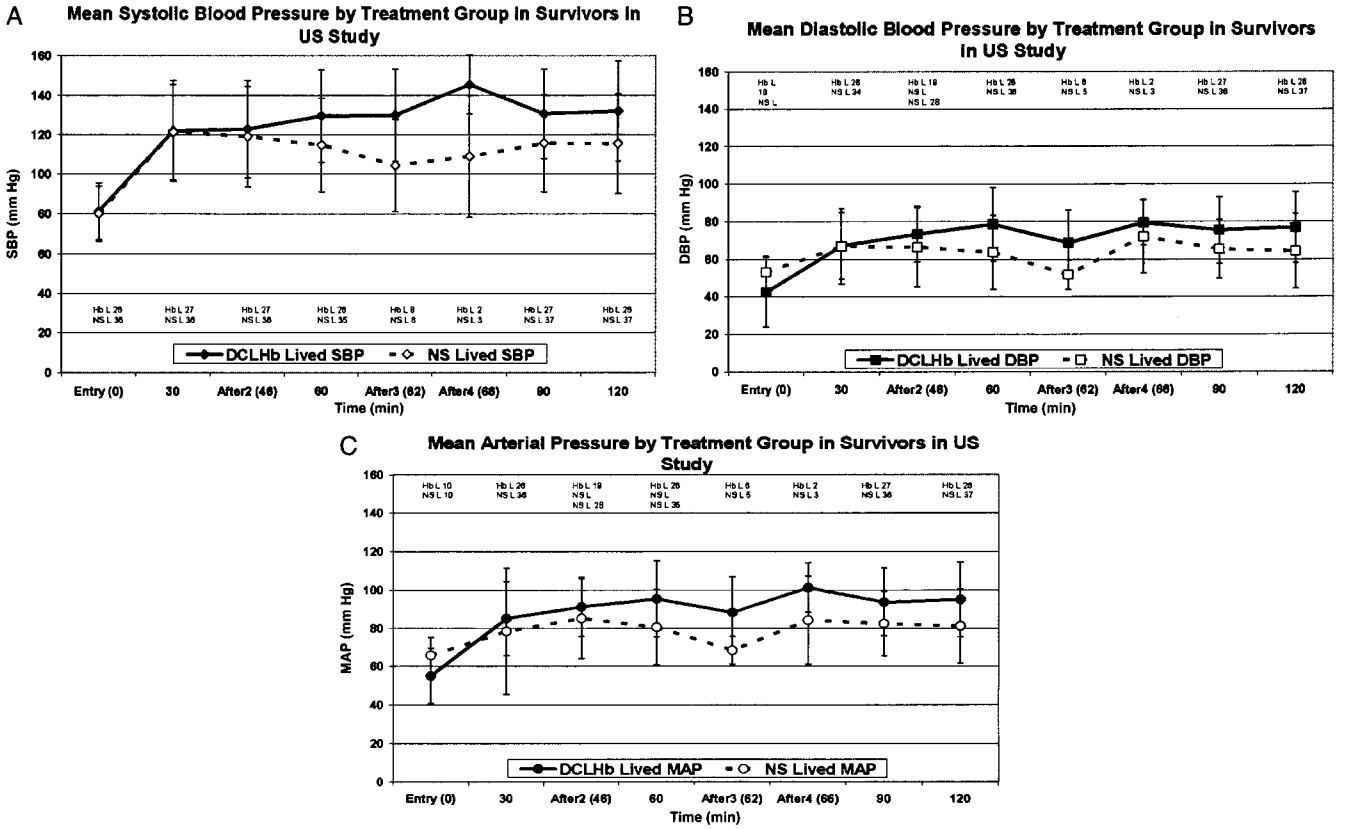

FIG. 5. **Blood pressure by treatment group in survivors in the US study.** A, Mean SBP by treatment group in survivors in US study. B, Mean DBP by treatment group in survivors in US study. C, MAP by treatment group in survivors in US study.

RTS, study (European Union versus United States), sex, and initial base deficit.

In regression analysis of the US study data alone, treatment group was not correlated with SBP, DBP, or MAP at any time point. In the EU study, only SBP at 15 min was significantly correlated to treatment group (-13.01 ± 6.06, $P < 0.05$), accounting for 4.8% of the SBP variability. However, initial SBP, initial base deficit, and total blood received were all more strongly correlated to SBP at this 15-min time point than was treatment group.

DISCUSSION

The search for a hemoglobin solution that could improve traumatic hemorrhagic shock patient outcomes both in the civilian and in the military setting has as of yet not been fruitful (18, 33–38). There is a continuing effort to develop a solution that can be carried by field medics or paramedics that is stable at room temperature and can be easily used in a broad population of traumatic hemorrhagic shock patients. The development of such a solution has been hampered in part by concerns regarding the potential adverse pressor effects of hemoglobin solutions and in particular DCLHb, a pure hemoglobin tetrameric solution (10, 19, 39–44).

The use of DCLHb and other oxygen carrying hemoglobin solutions with a pressor effect possibly could hinder successful patient resuscitation through several mechanisms. A pressor effect that raises systolic BP could accelerate hemorrhage because of a disruption in a haemostatic plug that had temporarily halted hemorrhage, either from an injured vessel or from an injured solid viscous such as the liver or the spleen. Because of a pressor effect, these products could also alter perfusion to vital organs such as the heart, the lungs, the liver, the kidney, and the brain in a way that could cause the occurrence of multisystem organ failure after the acute resuscitation, which could increase mortality over the first 28 days. This purported pressor effect could also complicate the resuscitation of traumatic hemorrhagic shock patients as elevations in SBP lead clinicians to underresuscitate these patients, causing worsening perfusion over time due to inadequate intravascular volumes. Lastly, a potential complication of the use of an HBOC could be the delay in the use of oxygen carrying solutions such as O-negative blood or crossmatched blood because clinicians have used a hemoglobin carrying solution as part of the initial resuscitation.

The use of these two DCLHb studies as a model for BP effects is an important one, given that this pure tetrameric DCLHb solution was tested as a therapeutic due to its consistent pressor effect (17, 24, 39). Although pressor effects are thought to be more consistently observed with DCLHb, a pure solution of hemoglobin tetramer, these pressor effects might also occur with other hemoglobin solutions such as

Hemolink, Hemopure (HBOC-201), Hemospan, or PolyHeme (8, 25, 27, 28, 31, 45–55). Similarly, if there is no clinically significant pressor effect measured with DCLHb, it might then be possible to infer that BP problems may be less likely with these nontetrameric solutions when used in the resuscitation of traumatic hemorrhagic shock patients.

The use of patient data from both the US and the EU studies effectively includes both penetrating and blunt trauma victims and addresses resuscitation both in the prehospital setting (EU study) and in the ED setting after the infusion of crystalloids by EMS paramedics (US study). The patients in these clinical trials were comparable to other trauma populations from othertraumatic hemorrhagic shock studies, with a similar blunt and penetrating trauma mix and overall mortality (56–58).

In the patient population combined from the US and EU studies, there was no consistent difference in BP over time based on treatment group. Although there were individual differences in the mean BPs at specific time points, the elevation in BP was not related to treatment with DCLHb, nor was it consistently observed over the entire 120-min resuscitation period. This lack of a consistent pressor effect as measured by BP readings in the clinical setting does not correlate with the observations from the clinical studies of DCLHb and other HBOCs (11–13, 15, 16, 49, 52).

There is a stated concern that a subset of patients may have an idiosyncratic reaction to DCLHb or to other hemoglobin solutions that would cause patients to have a pressor effect with SBP elevations to 160 mmHg or greater (10, 18, 59). In this study, there was no difference in the distribution of patients who had SBP readings 160 or 120 mmHg or greater based on treatment group in the combined study group or in either the US or the EU studies alone. This suggests the absence of a consistent idiosyncratic response to DCLHb that causes markedly elevated SBPs that either required treatment could theoretically exacerbate hemostasis or could worsen perfusion in these traumatic hemorrhagic shock patients.

Blood pressures from the combined studies and in the individual US and EU studies were noted to be markedly higher in patients who survived their trauma as compared with those who expired. This is consistent with the clinical observations that patients whose BPs normalize have reached some degree of homeostasis (compensated shock), allowing them to survive long enough to receive operative intervention or continued resuscitation in the critical care setting (58, 60–62). This observation suggests that the use of a hemoglobin solution such as DCLHb associated with a pressor effect that elevates SBP does not necessarily cause higher mortality due to loss of a haemostatic plug, worsening perfusion, or inadequate resuscitation. This analysis, however, is complicated by the fact that BP data did become unavailable in those patients who expired early, which limits the ability to determine with certainty that this would be the case for all traumatic hemorrhagic shock patients who could be resuscitated with such a hemoglobin solution.

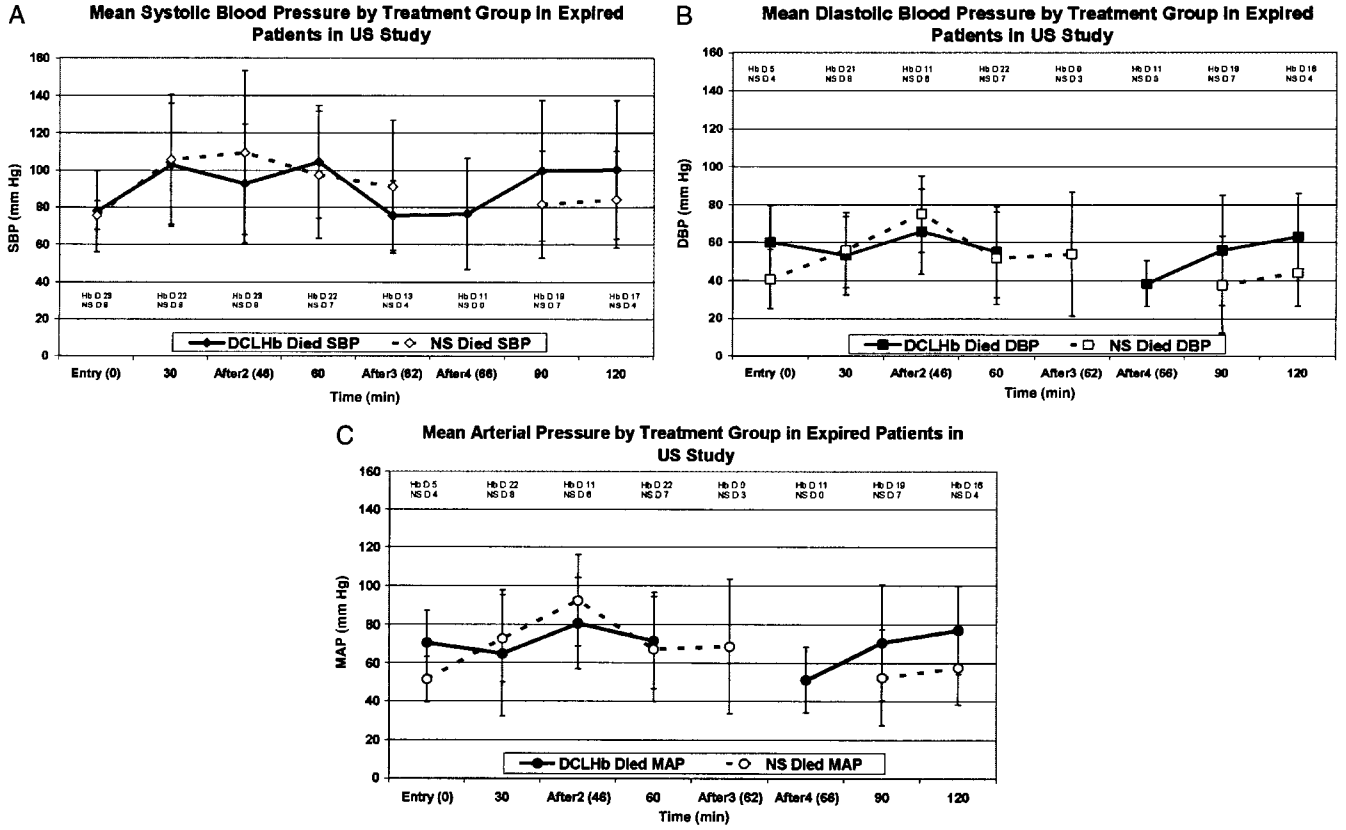

FIG. 6. **Blood pressure by treatment group in expired patients in the US study.** A, Mean SBP by treatment group in expired patients in US study. B, Mean DBP by treatment group in expired patients in US study. C, MAP by treatment group in expired patients in US study.

In an attempt to better understand the relationship between treatment with DCLHb in these two studies and the BP observations over time, individual analyses based on patient outcome were conducted for each of the US and EU studies. Although in the US study there were some differences in mean BP in those who survived their trauma between the two treatment groups, there were no consistently observed differences in those who expired after their trauma. Paradoxically, the few higher BP values observed in expired patients were in patients treated with NS and not in those treated with DCLHb. In the EU study, in which there was no difference in outcome based on DCLHb treatment, there were no BP differences in either treatment group based on outcome. These observations again suggest that there is no consistent clinically relevant BP effect either by treatment group or by patient outcome from either of the DCLHb studies.

The regression analysis data suggest only a minimal relationship between treatment group and SBP values over time. Treatment with DCLHb was not noted to be a primary predictor of SBP over time. Instead, more important were clinical variables such as overall injury severity and physiological findings at the time of the initial resuscitation such as baseline SBP, base deficit, GCS score, and initial Hb. This is consistent with the observation that the most important predictors of outcome are anatomic injury, physiologic status, and head injury, as measured by the GCS score (63–67).

The greatest limitation of this analysis is that the fact that some BP values, especially DBP, were not consistently available and the fact that as patients expired, their data were no longer available to be used in comparing BP over time. Also noted is the fact that BP values were collected at different times in the two clinical trials. Despite these facts, the ability to serially measure BP over time does allow the conclusion to be made that there was no consistent relationship between treatment group and BPs in these traumatic hemorrhagic shock patients.

In conclusion, the detailed analysis of BP data over the acute resuscitation period in patients treated for traumatic hemorrhagic shock in the US and EU clinical trials of DCLHb did not demonstrate consistent BP changes that could be related to a purported pressor effect of the DCLHb tetramer. The absence of a consistent pressor effect as demonstrated by BP over time suggests that the untoward outcome seen in DCLHb-treated patients in the US study and the absence of a benefit in the EU study could not be directly related to the pressor effect as measured by BP during the acute resuscitation period. Further analysis of perfusion data and shock index data will further elucidate whether this pressor effect is clinically relevant when hemoglobin solutions such as DCLHb are used in the treatment of traumatic hemorrhagic shock patients. This study and future analyses will hopefully allow further study of these hemoglobin solutions to be conducted in well-designed traumatic hemorrhagic shock clinical trials without significant concerns related to pressor effects that are thought to limit the effectiveness of these oxygen carrying solutions.

The finding that there is no demonstrable DCLHb pressor effect as measured by BP in two DCLHb traumatic hemorrhagic shock clinical trials will assist investigators as they attempt to clarify the further study and the potential use of HBOCs in clinical practice. It will also allow groups such as the Blood Products Advisory Committee and the FDA Center for Biologics Evaluation and Research who provide oversight to this process to fully understand what is known about DCLHb. This is especially important given the adverse outcome seen in the US DCLHb traumatic hemorrhagic shock clinical trial, which has been postulated, in part, to be due to the DCLHb pressor effect as well as the possibility of idiosyncratic BP effects that could cause certain patients to develop uncontrolled hypertension that causes significant morbidity, imparting a worse outcome. This study did not detect a consistent BP pressor effect, and it found no relationship between BP and patient outcome. It also did not find that patients treated with DCLHb sustained a large percentage of markedly elevated BP readings. These observations support the ongoing study of HBOCs as a resuscitation fluid in the management of traumatic hemorrhagic shock patients.

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APPENDIX

US DCLHb clinical efficacy trial

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